Claims

1. An isolated G-protein coupled receptor comprising an amino acid sequence which is at least 90% identical to a sequence selected from the group consisting of SEQ ID Nos. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, and 28.

2. An isolated G-protein coupled receptor comprising an amino acid sequence selected from the group consisting of SEQ ID Nos. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, and 28.

3. An isolated polynucleotide encoding a G-protein coupled receptor of claim 1 or 2.

4. The isolated polynucleotide of claim 3, wherein said polynucleotide encoding each of said G-protein coupled receptors of SEQ ID Nos. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, and 28, comprises the sequence of SEQ ID Nos. 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, and 27, respectively.

5. A nucleic acid vector comprising a polynucleotide sequence selected from the group consisting of SEQ ID Nos. 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, and 27.

6. A cell comprising the nucleic acid vector of claim 5.

7. The cell of claim 6 wherein the polynucleotide sequence of said expression vector is expressed in the cell membrane of said cell.

8. A non-human mammal having a homozygous null mutation in the gene encoding a polynucleotide selected from the group consisting of SEQ ID Nos. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, and 28.

9. A non-human mammal transgenic for a polynucleotide encoding a G-protein coupled receptor, wherein said polynucleotide is selected from the group consisting of SEQ ID Nos. 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, and 27.

10. A method of identifying an agent that modulates the function of GPCRx11, said method comprising:

(a) contacting a GPCRx11 polypeptide with angiopeptin in the presence and absence of a candidate modulator under conditions permitting the binding of said angiopeptin to said GPCRx11 polypeptide; and

(b) measuring the binding of said GPCRx11 polypeptide to said angiopeptin, wherein a decrease in binding in the presence of said candidate modulator, relative to the binding in the absence of said candidate modulator, identifies said candidate modulator as an agent that modulates the function of GPCRx11.

11. A method of detecting, in a sample, the presence of an agent that modulates the function of GPCRx11, said method comprising :

(a) contacting a GPCRx11 polypeptide with angiopeptin in the presence and absence of said sample under conditions permitting the binding of said angiopeptin to said GPCRx11 polypeptide; and

(b) measuring the binding of said GPCRx11 polypeptide to said angiopeptin , wherein a decrease in binding in the presence of said sample, relative to the binding in the absence of said sample, indicates the presence, in said sample of an agent that modulates the function of GPCRx11.

12. A method of identifying an agent that modulates the function of GPCRx11, said method comprising :

(a) contacting a GPCRx11 polypeptide with angiopeptin in the presence and absence of a candidate modulator; and

(b) measuring a signaling activity of said GPCRx11 polypeptide, wherein a change in the activity in the presence of said candidate modulator relative to the activity in the absence of said candidate modulator identifies said candidate modulator as an agent that modulates the function of GPCRx11.

13. A method of identifying an agent that modulates the function of GPCRx11, said method comprising:

(a) contacting a GPCRx11 polypeptide with a candidate modulator;

(b) measuring a signaling activity of said GPCRx11 polypeptide in the presence of said candidate modulator; and

(c) comparing said activity measured in the presence of said candidate modulator to said activity measured in a sample in which said GPCRx11 polypeptide is contacted with angiopeptin at its $EC_{50}$, wherein said candidate modulator is identified as an agent that modulates the function of GPCRx11 when the amount of said activity measured in the presence of said candidate modulator is at least 20% of the amount induced by said angiopeptin present at its $EC_{50}$.

14. A method of detecting the presence, in a sample, of an agent that modulates the function of GPCRx11, said method comprising :

(a) contacting a GPCRx11 polypeptide with angiopeptin in the presence and absence of said sample;

(b) measuring a signaling activity of said GPCRx11 polypeptide; and

(c) comparing the amount of said activity measured in a reaction containing GPCRx11 and angiopeptin without said sample to the amount of said activity measured in a reaction containing GPCRx11, angiopeptin and said sample, wherein a change in said activity in the presence of said sample relative to the activity in the absence of said sample indicates the presence, in said sample, of an agent that modulates the function of GPCRx11.

15. A method of detecting the presence, in a sample, of an agent that modulates the function of GPCRx11, said method comprising:

(a) contacting a GPCRx11 polypeptide with said sample;

(b) measuring a signaling activity of said GPCRx11 polypeptide in the presence of said sample; and

(c) comparing said activity measured in the presence of said sample to said activity measured in a reaction in which said GPCRx11 polypeptide is contacted with angiopeptin present at its $EC_{50}$, wherein an agent that modulates the function of GPCRx11 is detected if the amount of said activity measured in the presence of said sample is at least 20% of the amount induced by said angiopeptin present at its $EC_{50}$.

16. The method of any one of claims 1-6 wherein said angiopeptin is detectably labeled.

17. The method of claim 16 wherein said angiopeptin is detectably labeled with a moiety selected from the group consisting of a radioisotope, a fluorophore, a quencher of fluorescence, an enzyme, and an affinity tag.

18. The method of any one of claims 10-15 wherein said contacting is performed in or on a cell expressing said GPCRx11 polypeptide.

19. The method of any one of claims 10-15 wherein said contacting is performed in or on synthetic liposomes.

20. The method of any one of claims 10-15 wherein said contacting is performed in or on virus-induced budding membranes containing a GPCRx11 polypeptide.

21. The method of any one of claims 10-15 wherein said method is performed using a membrane fraction from cells expressing said GPCRx11 polypeptide.

22. The method of either of claims 10 or 11 wherein said measuring is performed using a method selected from label displacement, surface plasmon resonance, fluorescence resonance energy transfer, fluorescence quenching, and fluorescence polarization.

23. The method of any one of claims 10-15 wherein said agent is selected from the group consisting of a peptide, a polypeptide, an antibody or antigen-binding fragment thereof, a lipid, a carbohydrate, a nucleic acid, and a small organic molecule.

24. The method of any one of claims 12-15 wherein said step of measuring a signaling activity of said GPCRx11 polypeptide comprises detecting a change in the level of a second messenger.

25. The method of any one of claims 12-15 wherein the step of measuring a signaling activity comprises measurement of guanine nucleotide binding or exchange, adenylate cyclase activity, cAMP, Protein Kinase C activity, phosphatidylinosotol breakdown, diacylglycerol, inositol triphosphate, intracellular calcium, arachinoid acid, MAP kinase activity, tyrosine kinase activity, or reporter gene expression.

26. The method of claim 25 wherein said measuring a signaling activity comprises using an aequorin-based assay.

27. A method of identifying a molecule which binds to a G-protein coupled receptor comprising:

(a) contacting a G-protein coupled receptor having an amino acid sequence selected from the group consisting of SEQ ID Nos. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, and 28, with a candidate molecule;

(b) measuring the binding of said G-protein coupled receptor to said candidate molecule, wherein a detectable level of binding indicates that said candidate molecule binds to said G-protein coupled receptor.

28. The method of claim 27, wherein said candidate molecule is detectably labeled.

29. The method of claim 28, wherein said candidate molecule is detectably labeled with a moiety selected from the group consisting of a radioisotope, a fluorophore, a quencher of fluorescence, an enzyme, and an affinity tag.

30. The method of claim 27, wherein said measuring is performed using a method selected from label displacement, surface plasmon resonance, fluorescence resonance energy transfer, fluorescence quenching, and fluorescence polarization.

31. A method of identifying a ligand for a G-protein coupled receptor comprising:

(a) contacting a G-protein coupled receptor having an amino acid sequence selected from the group consisting of SEQ ID Nos. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, and 28, with a candidate ligand;

(b) measuring a signaling activity of said G-protein coupled receptor in the presence of said candidate ligand, wherein a ligand for said G-protein coupled receptor is identified if an increase in said signaling activity is measured in the presence of said candidate ligand relative to said signaling activity in the absence of said candidate ligand.

32. The method of claim 31, wherein said candidate ligand is detectably labeled.

33. The method of claim 27 or 31, wherein said contacting is performed in or on a cell expressing said G-protein coupled receptor.

34. The method of claim 27 or 31, wherein said contacting is performed in or on synthetic liposomes.

35. The method of claim 27 or 31, wherein said contacting is performed in or on virus-induced budding membranes containing said G-protein coupled receptor.

36. The method of claim 27 or 31, wherein said method is performed using a membrane fraction from cells expressing said G-protein coupled receptor.

37. The method of claim 31 wherein said step of measuring a signaling activity of said G-protein coupled receptor comprises detecting a change in the level of a second messenger.

38. The method of claim 31 wherein the step of measuring a signaling activity comprises measurement of guanine nucleotide binding or exchange, adenylate cyclase activity, cAMP, Protein Kinase C activity, phosphatidylinosotol breakdown, diacylglycerol, inositol triphosphate, intracellular calcium, arachinoid acid, MAP kinase activity, tyrosine kinase activity, or reporter gene expression.

39. The method of claim 31 wherein said measuring a signaling activity comprises using an aequorin-based assay.

40. A method of modulating the activity of a GPCRx11 polypeptide in a cell, said method comprising the step of delivering to said cell an agent that modulates the activity of a GPCRx11 polypeptide, such that the activity of GPCRx11 is modulated.

41. A method of diagnosing a disease or disorder characterized by dysregulation of GPCRx11 signaling, said method comprising :

(a) isolating nucleic acid from a tissue sample;

(b) amplifying a GPCRx11 polynucleotide, using said nucleic acid as a template; and

(c) comparing the amount of amplified GPCRx11 polynucleotide produced in step (b) with a standard, wherein a difference in said amount of amplified GPCRx11 polynucleotide relative to said standard is diagnostic of a disease or disorder characterized by dysregulation of GPCRx11.

42. A composition consisting essentially of an isolated GPCRx11 polypeptide and isolated angiopeptin.

43. A kit for screening for agents that modulate the activity of GPCRx11, said kit comprising an isolated GPCRx11 polypeptide and isolated angiopeptin.

44. A kit for screening for agents that modulate the activity of GPCRx11, said kit comprising isolated angiopeptin and a cell membrane fraction comprising a GPCRx11 polypeptide.

45. A kit for screening for agents that modulate the activity of GPCRx11, said kit comprising an isolated polynucleotide encoding a GPCRx11 polypeptide and isolated angiopeptin.

46. A kit for screening for agents that modulate the activity of GPCRx11, said kit comprising a cell transformed with a polynucleotide encoding a GPCRx11 polypeptide and angiopeptin.

47. A kit for the diagnosis of a disease or disorder characterized by dysregulation of GPCRx11 signaling, said kit comprising an isolated polynucleotide encoding a GPCRx11 polypeptide, a standard and packaging materials therefor.

48. The kit of claim 47 which further comprises angiopeptin.

49. A kit for the diagnosis of a disease or disorder characterized by dysregulation of GPCRx11 signaling, said kit comprising a cellular membrane fraction comprising a GPCRx11 polypeptide, a standard and packaging materials therefor.

50. The kit of claim 49 which further comprises angiopeptin.

51. The kit of claim 49 wherein said standard comprises a sample from an individual not affected by said disease or disorder.

52. A kit for the diagnosis of a disease or disorder characterized by dysregulation of GPCRx11 signaling, said kit comprising a cell transformed with a polynucleotide encoding a GPCRx11 polypeptide, a standard and packaging materials therefor.

53. The kit of claim 52, further comprising angiopeptin.

54. The kit of claim 53 wherein said standard comprises a sample from an individual not affected by said disease or disorder.